FDA's Drug Approval Process: Up to the Challenge?
Bill Number:
Hearing Date: March 1, 2005, 9:30 am
Location: SD106
Witness:
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Testimony

I. Introduction

Chairman Enzi, Senator Kennedy, and distinguished members of the Committee, I thank you for the opportunity to discuss the FDA's drug approval process, and its impact on the availability of safe and effective tools for combating devastating diseases like cancer.

My name is Nancy Davenport-Ennis, and I am the CEO of The National Patient Advocate Foundation. We serve as a strong advocate for policy and legislative reforms that eliminate barriers to patient access to treatment. Although I am not an expert in the regulatory processes at FDA or the enabling statutes that govern them, I can speak with considerable authority about how patients and survivors view the FDA both today and from a historical standpoint, and what issues like risk, benefit, and timely access mean to those suffering from life altering conditions.

I stand before you as a two-time cancer survivor. Not only have I experienced the burden of this disease first hand, it also has taken the lives of close friends and family members.

I know that many of you on the committee and in the room here today have been touched by cancer as well. According to the American Cancer Society, one out of every two men and one out of every three women will have some type of cancer. An estimated 564,000 people died from cancer in 2004. Cancer has recently surpassed heart disease as the leading cause of death among people under the age of 85.

Although I advocate on behalf of patients with a multitude of life altering diseases, it is against this backdrop of cancer's enormous burden and threat that I would like to offer the committee my thoughts on the FDA's approval process. I would also like to acknowledge that my testimony was developed in partnership with my colleagues at the Friends of Cancer Research -- a non-profit organization that raises awareness and provides public education on cancer research in order to accelerate the nation's progress toward better tools for the prevention, detection, and treatment of cancer.

Both of our organizations take pride in knowing that we work on behalf of patients not only to improve access and quality of care, but also to support a strong national commitment to the research and development necessary to produce innovative medical tools that are both safe and effective

II. Understanding the Cancer Perspective on Safety and Efficacy

Cancer is a cellular disease that begins in the body long before physical symptoms are usually expressed. Because it is difficult to catch many cancers early (when the disease is often easier to treat and survival rates are typically much higher), many diagnoses come in the later stages of disease where the symptoms are rapidly becoming more acute and the long-term survival prospects are grim. The conventional way of stopping the cancerous cells from spreading is to eradicate them either through surgery, radiation therapy, chemotherapy, or some combination of these options. Many of the cancer drugs used to stop the disease from spreading are unable to discriminate between the cancerous cells and the non-cancerous cells. A great number of healthy cells are consequently destroyed in the treatment process, which can bring uncomfortable and sometimes painfully disabling side effects. Thus, cancer often presents the patient and the physician with the painful tradeoff between burden of treatment and burden of disease.

Cancer patients understand all too well that there is no such thing as a drug that is 100% safe. Virtually all approved drugs and biologics have near term side effects and carry some risk. Most agents also pose known and unknown risks associated with chronic use and delayed toxicity. The severity of those side effects and the level of risk will vary from person to person, and from agent to agent. The question is not whether a drug is completely safe or completely effective, but rather how effective is it compared to how safe it is. This risk-benefit balance is the essence of the FDA's review process.

The agency evaluates the risk versus the benefit of a proposed product using a scientifically derived process conducted by experts with the knowledge and judgment necessary to assess the balance between the two. Most importantly, these experts typically have a working knowledge of the condition the product is designed to address so the impact of disease is not overlooked when considering safety and efficacy.

The FDA's review of oncology products differs from its review of other medicinals in that efficacy is often of greater concern than toxicity. While safety is always considered in the review and product label, significant toxicity is generally considered acceptable for oncology drugs given the severe and often fatal nature of the disease being treated.

This approach to the review of oncology products is generally consistent with the manner in which cancer patients and their physicians select from a complex array of treatment options. The safety of a drug or other treatment option is not considered in isolation, but rather the risk of side effects is weighed against the potential benefits a particular course of treatment may provide compared to the risk from spread of disease. The decision about whether or not to deploy powerful and sometimes risky medications in an effort to improve the life of a cancer patient ultimately rests with that particular patient and their prescribing physician.

But because the burden of cancer is usually far more damaging and toxic than the

interventions used to stop it, many patients and their caregivers place a premium on the rate at which cancer products are approved and the subsequent access to those products.

As a former cancer patient, I can assure you that time is a very precious commodity to someone diagnosed with cancer. The FDA's capacity to effectively evaluate safety and efficacy is just as critical as the speed at which that evaluation is conducted. When you are suffering from cancer and your expected life span may be months or even weeks, you shouldn't have to wait any longer than is necessary for the FDA to approve new medical products.

It is for that reason that many advocacy organizations across the disease community were so supportive of the Prescription Drug User Fee Act (PDUFA).

III. The Impact of PDUFA

PDUFA initially had 2 primary objectives: 1) reduce the time required for FDA review of new drug and biological product applications, and 2) thereby enable patients to have earlier access to new therapies. Under PDUFA, the FDA collects user fees from industry to supplement annual appropriations for review of new drug applications. According to the Government Accountability Office (GAO), between 1993 – when PDUFA was first implemented – and 2001, FDA utilized user fees to increase its medical and scientific drug review personnel by 77 percent. Thanks to the additional resources and staff provided by this legislation and its subsequent versions, the agency has cut nearly in half its 27-month median approval time for standard drugs. This accomplishment means that patients gain access to new drug therapies significantly sooner than they otherwise would.

Based upon an analysis of data available on the FDA's website, the agency approved 953 new drug applications (NDAs) between 1993 and 2003. The average total time for the approval of those applications that underwent "standard review" (745 of the 953) was 26.9 months in 1993 compared to 15.4 months in 2003. The average total time for the approval of those applications that underwent "priority review" (208 of the 953) was 16.3 months in 1993 compared to 7.7 months in 2003. Pursuant to the Food and Drug Administration Modernization Act (FDAMA) of 1997, "priority review" is a designation intended for those products that address unmet medical needs.

For those drugs classified as new molecular entities (NMEs), a term used to describe an active ingredient that has never been marketed in this country, the agency approved 321 applications between 1993 and 2003. The average total time for the approval of those NME applications that underwent "standard review" (192 of the 321) was 27.2 months in 1993 compared to 23.1 months in 2003. The average total time for the approval of NME applications that underwent "priority review" (129 of the 953) was 14.9 months in 1993 compared to 6.7 months in 2003.

Thanks to improvements made in the pace of the FDA's review process over the past decade or so, thousands of cancer patients have had earlier access to new cancer treatments. Consequently, many cancer patients' lives have been extended or their quality of life improved.

For example, according to information found in the FDA's FY 2006 Budget Summary:

"a new biologic for the / trastuzumab) was approved by FDA in less®treatment of breast cancer (Herceptin than 5 months. This drug took 18 months to be approved in Europe. There were an estimated 10,000 American patients with advanced breast cancer who received this / trastuzumab) during the time that FDA might have®new treatment (Herceptin still been reviewing the application, had it not been for the improvements made possible with the additional funds under PDUFA. This added an estimated 2300 years of life to the population who had access to the new treatment /trastuzumab) following its market approval in May of 1998."®(Herceptin

In making it possible for drugs deemed safe and efficacious to make it to market more quickly, PDUFA has made the difference between life and death for many patients with cancer or other life-threatening illnesses.

IV. We Stand on the Threshold of Incredible Advances in Cancer Research

We are entering an especially exciting time with respect to the development of innovative drug treatments. In recent years, the FDA approved several pharmaceutical products that treat cancer in entirely new ways, such as Avastin® and Erbitux® for treatment of colorectal cancer and Tarceva® for lung cancer.

Incredible progress in fields such as genomics and proteomics has vastly increased our knowledge about cancer's molecular and genetic signals and processes. Such information allows for the detection of cancer at a much earlier stage, when treatment options are often more numerous, less invasive, and more successful. Cancer research also is moving us closer to more targeted treatments, whereby advanced technology can be used to target and destroy cancerous cells without damaging the body's healthy cells. Finally, the scientific foundation has been laid for the technological capacity to prevent cancer growth altogether by blocking or interfering with the molecular signals that turn healthy cells into cancerous cells.

We look to the National Institute's of Health, our nation's many academic research institutions and community oncology practices, in addition to pharmaceutical and biotech firms to invest an enormous level of resources into Research and Development in order to develop better tools for preventing disease, detecting it sooner, and treating it more effectively.

We then look to the FDA to serve as a gatekeeper for the entry of those products into the market so that patients have access to those deemed "safe and effective." Once those products are approved, we rely upon the agency to provide sufficient information about a product's risks and benefits so that patients and their caregivers are empowered to make personalized decisions about their care.

With literally hundreds of oncology products now in the developmental pipeline, the demand upon FDA for advice and review will rapidly accelerate. Thus, the agency's

regulatory oversight of cancer research must be as rationally and efficiently structured as possible in order to insure timely delivery of cutting edge science to patients.

The FDA took a positive step in the right direction last July when it announced the formation of an Oncology Office that would allow for better consolidation and integration of the Agency's cancer-specific expertise. The Interagency Oncology Task Force formed between FDA and the National Cancer Institute in 2003 also has been a positive step toward enhancing the efficiency of clinical research and the scientific evaluation of new cancer medications. Through this program, federal researchers and regulators have been developing ways to share knowledge and resources that will accelerate the development of new cancer drugs that are safe and effective.

However, we are deeply concerned that potential efforts to legislate unrealistically heightened degrees of certainty with respect to the safety of drugs could turn back the clock on what we view as important reforms in terms of improved efficiency and accelerated access to vital drug therapies achieved by the FDA. Our patients simply cannot afford unduly burdensome regulatory or bureaucratic requirements that could halt such progress or unravel the gains made since enactment of PDUFA.

V. Be cautious with safety

We appreciate the Committee's scrutiny of recent concerns regarding drug safety, and we share your commitment to assuring that information about risks associated with drugs is identified and disseminated as early as practicable. However, it is important to always keep in mind that beneficial drug products are going to have associated with them a certain amount of risk. Aspirin has risks; penicillin has risks; the vaccines we give our babies to immunize from disease like polio and diphtheria carry risk. No drug is ever 100% safe.

Just like patients and their caregivers must weigh the benefits and risks associated with a particular product when deciding whether or not to use it to fight or prevent disease, we feel that the FDA must continue to carefully weigh the benefits and risks associated with a product when deciding whether or not to grant approval. For that reason, we would advise against any effort that creates new regulations or bureaucracy that isolates or further separates either the drug safety function or the drug efficacy function from the overall drug review process. Safety and efficacy must never be viewed in isolation from each other. The FDA's review process should remain structured in a way that emphasizes the benefit-risk balance of a medicine as a basis for approval.

Drug reviews that are not based on this delicate balance will almost certainly discourage research on new therapies for dread diseases like cancer and AIDS. It may become very difficult to get a drug approved for cancer treatment if the regulatory hurdles for safety are too high because those drugs are likely to have some level of side effects, and they are likely to be used in a patient population that is sick and vulnerable to adverse reactions. Of even greater concern is how an overemphasis on safety might have a devastating

impact on the advancements being made in our ability to detect cancer early or prevent it altogether. Remember, cancer is a biological process that starts in the body years or even decades before a diagnosis is made. The ability to detect that process early or stop it all together represent our greatest hope for significantly reducing or eliminating the suffering and death due to cancer. The conundrum is that the clinical testing and medical application of new technologies for early detection and prevention will involve people at risk for cancer who are not yet showing signs of advanced disease and may be entirely without symptoms. However, the tools for early detection and prevention are going to have side effects, just like any medical intervention. If the regulatory hurdles for safety are too high, it will be very difficult to get new tools for prevention and early detection approved even though they may save hundreds of thousands, if not millions, of lives in the not too distant future.

And who is going to pour billions of dollars into the research and development of new cancer products if they are not likely to be approved because they might not be considered safe enough irregardless of their benefits, or if they will face an even longer and less efficient review process?

VI. What we support

Of course the FDA's role in evaluating and monitoring safety should be strengthened. But more importantly, we want safer and more effective drugs moved through the system as efficiently as possible so they can be used as soon as possible by those who need them most, such as cancer patients and/or those at high risk for cancer.

We would prefer strategies and solutions designed to improve the FDA's capacity in the areas of safety, efficacy, and efficiency simultaneously. At the very least, any effort to improve one aspect of these factors alone should not be implemented without careful consideration of how the other two might be impacted. And this means that FDA's budget must be considered accordingly.

The following are the 5 key "Pillars of Safety" that we think are critical to reforms at the FDA:

1- Safety and Efficacy must continue to be the foundational elements of the FDA regulatory process. Safety cannot exist in a vacuum apart from efficacy.

2- Mechanisms to enhance existing structures and processes for post market safety monitoring and adverse event reporting must be explored.

3- Efforts to bring even greater efficiency and scientific expertise to the FDA's review and monitoring processes must continue; such efforts must be done in a manner that empowers the Agency to keep pace with the rapid advancements now occurring in areas such as genomics, proteomics, and nanotechnology.

4- FDA must continue to work with industry, patient groups, physicians, hospitals, academia, and other government agencies to enhance the critical path.

5- The FDA must be sufficiently resourced in order to insure more effective pursuit of its existing mandates. Additional resources are even more essential if FDA is to successfully implement a comprehensive suite of reforms.

We are encouraged by FDA's plan to allocate more than $70 million over five years to support enhanced monitoring and surveillance of risks that may be associated with drug products already on the market. However, no drug is without risk; and it always has been an unfortunate but unavoidable fact that some adverse effects may not become apparent until after a drug has been in wide or extended use. We can hope to minimize such adverse effects and enhance the agency's capacity to report them, but we must also accept certain risks associated with beneficial drug products. Moreover, without new monies, every dollar the FDA shifts towards new regulations and infrastructure for safety is money taken away from programs that allow the agency to more effectively and efficiently evaluate risk and benefit together.

Finally, one of the keys to a stronger FDA and a more robust development pipeline is a clear plan for how the agency will work to modernize the medical product development process. We are pleased that such a proposal has been presented in the recently published report:
"Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products." This document details the agency's plan to update the tools currently used to assess the safety and efficacy of new medical products. We fully support the FDA's willingness to reach out to numerous stakeholders in an effort "to coordinate, develop, and/or disseminate solutions to scientific hurdles that are impairing the efficiency of product development industry-wide."

V. In Conclusion

We welcome the recent discussions about how we can make our drug approval system better, but we are mindful of the fact that patients with life altering diseases like cancer are given hope because of the advances of scientific discovery and development. We support reform that makes drugs safer, but warn against those that might unintentionally slow down the flow of better technology for treatment, prevention, and detection -- or worse, discourage their creation altogether. The only way to prevent such intended consequences is to have a thoughtful policy discussion not about safety alone, but safety in combination with benefit and efficiency. While we of course want safer drugs, we feel that any safety reforms absolutely must be matched with efforts to enhance the FDA's the level of efficiency, scientific expertise, and overall capacity to fulfill its numerous mandates.